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BACPAC I Draft Guidance Comments – Geneva Pharmaceuticals

DOCKET # 98D-0994

All comments will be referred to by line number.

I. Introduction

Lines 7-8: Clarification is needed as to the exact relationship of intermediates to the synthetic pathway. Suggested that "used" be inserted after "intermediates."

Line 15: Questioned whether a change in manufacturer of a starting material is included in BACPAC I.

Lines 21-24: For clarification, suggested that "for specified postapproval changes" be moved to right after "information."

Lines 32-48: Suggested that these two paragraphs belong prior to, or at least at, the beginning of the intro section.

II. General Considerations

Line 57: To eliminate contradiction, suggested that language about final intermediate be reiterated from lines 14-15.

Lines 66-79: Major issues with this paragraph such as:

- What specifically is required from the DMF holder and applicant and what are each of their responsibilities? Maybe a chart/tree would be helpful.

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- How much information could the DMF holder keep confidential if the applicant needs info to file?
- If a change falls under BACPAC I and the DMF holder files all changes according to BACPAC I, is it necessary for the applicant to file more than a general reference to this change in an annual report? Only when changes fall under BACPAC II, should the applicant be obligated to file more info and provide a more thorough review.
- The paragraph is attempting to cover NDA and ANDA scenarios and seems to be too vague.

III. Assessment of Change

Lines 89-91: It is not clear in this sentence why drug product might be put up on stability. Suggested that "...stability problems may potentially occur, the first commercial..." be replaced by "...equivalence is not demonstrated, a representative..." It was also suggested that "considered to be" be inserted between "be" and "included" and that "based upon assessment of product stability" be added to the end of the sentence.

A. Equivalence of Impurity Profiles

Line 124: Concern for specifying "...range of historical data from *ten* premodification commercial batches." Ten lots of data may not be feasible much of the time. It was suggested that "if available" be added after "...batches" and that in the Glossary (lines 591-593), the sentence in italics be removed.

Lines 163-166: What is the ANDA holder's responsibility if the vendor has determined equivalence of an outsourced intermediate? Does this apply to starting materials?

IV. Types of Change

A. Site, Scale, and Equipment Changes

1. Site Changes

Lines 217-226: This doesn't seem to apply to a change in supplier of starting materials. It should be clearer, although we think it does.

Lines 232-233: On these lines and others throughout the document, it is not clear whether both the DMF holder and the ANDA holder have to file. If they don't always have to, then in what instances would this be the case? Also lines 279-280.

Line 240: Who's report are they referring to? Can we use DMF holder's report?

Line 262: Who's annual report are they referring to?

2. Scale Changes

Lines 288-289: What does "description of the source of the historical data" mean?

Lines 305-306: This isn't clear. If "outsourced" means the RM mfr's source, why would a scale change at the mfr's site affect the outsourced intermediate? This seems to be saying that only if the scale change happens at the outsourced intermediate mfr plant do we need a C of A. Also for line 439.

A. Specification Changes

This entire section seems to be focused on the RM mfr, not the ANDA holder.

B. Manufacturing Process Changes

Lines 503-505: We are not sure what is meant by this "change-control protocol."

Attachment A – BACPAC Decision Tree

In its current state, this decision tree provides very little assistance. A more comprehensive decision tree, outlining the whole document would be of greater use.

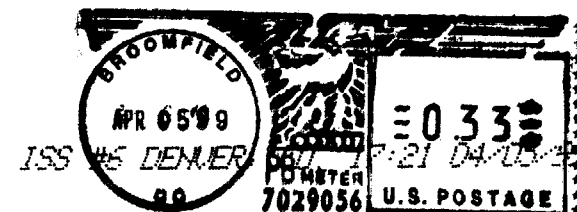
Attachment B – Glossary of Terms

The only comment was for the term "Historical Data" (refer to comments for line 124).



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